COMPARISON OF THE HEMODYNAMIC EFFECTS OF TWO ANESTHETIC INDUCTION PROTOCOLS ON ASA I-ASA II PATIENTS UNDERGOING ELECTIVE SURGERY[1]

COMPARACIÓN DE DOS TÉCNICAS ANESTÉSICAS SEGÚN EL COMPORTAMIENTO HEMODINÁMICO DURANTE LA INDUCCIÓN EN PACIENTES CON ASA I-ASA II LLEVADOS A CIRUGÍA ELECTIVA BAJO ANESTESIA GENERAL

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Abstract

Objectives: Choosing the best induction technique used on each patient is a process that involves the analysis of the patient's comorbid conditions and their hemodynamic effects, i.e. the effect on heart rate, arterial blood pressure, end-tidal carbon dioxide, oxygen saturation and mean arterial pressure during induction.

This study aims to compare two anesthetic protocols commonly used during anesthetic induction: propofol and ketamine vs. propofol and fentanyl in patients undergoing elective surgery.

Methods: A cross-sectional study was performed between September, 2013, and January, 2014, including all patients ASA I-II undergoing elective surgery; it was a convenience sample with a ratio of 1:1.

Resumen

Objetivo: La técnica anestésica utilizada en cada paciente es diferente según sus enfermedades concomitantes y se escoge con el fin de disminuir posibles efectos hemodinámicos, como alteraciones de la frecuencia cardiaca y la tensión arterial durante la inducción. En el presente estudio se pretendió comparar dos técnicas anestésicas, propofol-ketamina frente a propofol-fentanilo, en pacientes llevados a cirugía electiva.

Metodología: Se llevó a cabo un estudio de corte transversal entre septiembre de 2013 y enero de 2014, que incluyó todos los pacientes con ASA I-II. Se hizo un muestreo por conveniencia con una relación de 1:1.

Resultados: Se incluyeron 60 pacientes, 30 recibieron propofol-ketamina y 30 recibieron propofol-fentanilo. Las

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Results: A total of 60 patients were included, 30 received propofol and ketamine and 30 patients received propofol and fentanyl, both groups were comparable. The risk of bradycardia at minute 5 was measured on each group; on the group receiving propofol and fentanyl was OR=7.2 (95% CI 1.81-64.4) p=0.005, and the risk of tachycardia with propofol and ketamine OR=14.5 (95% CI 1.7 - 122) p=0,002.

Changes in mean arterial pressure were only significant during the first five minutes for both groups.

Conclusion: The combination of fentanyl and propofol is more likely to produce bradycardia and hypotension while propofol and ketamine is more likely to generate hypertension and tachycardia. Larger studies are needed to establish what the best induction protocol.

Keywords: Propofol, ketamine, fentanyl, hypotension.

poblaciones eran comparables. El riesgo de bradicardia con propofol-fentanilo al minuto cinco, mostró OR=7.2 (IC95% 1.81-64.4) (p=0,005); el riesgo de taquicardia con propofol-ketamina al minuto cinco, mostró OR=14.5 (IC95% 1.7-122) (p=0,002). Las alteraciones de la tensión arterial media solo fueron significativas durante los cinco primeros minutos para ambos grupos.

Discusión: La técnica anestésica con propofol-fentanilo tiene mayor probabilidad de producir bradicardia e hipotensión, mientras que la técnica con propofol-ketamina tiene mayor probabilidad de generar hipertensión y taquicardia. Se requieren estudios más amplios para establecer cuál es la mejor técnica anestésica.

Palabras clave: propofol, ketamina, fentanilo, hipotensión.

INTRODUCTION

Patients undergoing general anesthesia require an anesthetic plan tailored according to their comorbid conditions. This plan seeks to raise the technique that provides greater hemodynamics stability, to keep pressures of perfusion of different organs and an adequate control of the autonomic nervous system (1).

One of the associated effects associated with the use of various drugs used during anesthetic induction is the presence of hypotension and bradycardia, making induction a period of increased hemodynamic vulnerability due to the depressant effects of anesthetics on the cardiovascular system which can translate into increased morbidity and mortality during anesthesia (2,3).

Despite the wide availability of inducing agents, the right combination of drugs that maintain hemodynamic stability has not been elucidated. The use of a combination of propofol and fentanyl during the induction phase is common in current clinical practice. However, there are associated effects in blood pressure and heart rate that can be undesirable. Anesthetic induction using ketamine in patients with hemodynamic instability is a common practice thanks to the effects observed on systemic vascular resistance and cardiac output making ketamine a medication with more favorable pharmacological properties that provides hemodynamic stability when used appropriately in patients who do not have contraindications to its use.

In an attempt to look for alternatives to avoid the hemodynamic depressing effects of the combination of fentanyl and propofol we implemented the use of ketamine as co-inductor looking for better hemodynamic profile.

Knowing the hemodynamic changes associated with the use of combinations like propofol and fentanyl compared to those of propofol and ketamine used as induction agents on ASA I and ASA II patients that require elective surgery can lead to the identification of hemodynamic changes, to the prediction of outcomes and the proposal of guidelines that can be used during the administration of anesthesia in our population.

METHODS

We reviewed the hemodynamic parameters documented on patients between September 2013, and January 2014, at the Hospital Simc parameters documented on patients between s likeving 60 patients classified as ASA I - ASA II (American Society of Anesthesiologists physical status classification) undergoing elective surgery under general anesthesia. We included patients ASA I-ASA II, with ages between 18 and 65 years undergoing any elective surgery, excluding pregnant women, critically ill patients, those with

history of psychiatric illness, and those with increased ocular pressure, hypertensive crisis, known coronary artery disease, pulmonary hypertension or brain injury.

The patients were divided in two groups: those who received propofol and ketamine (n=30) during anesthetic induction, and those who received propofol and fentanyl (n=30). Hemodynamic parameters like heart rate (HR), arterial blood pressure (BP), mean arterial pressure (MAP), oxygen saturation (SpO2) and end-tidal carbon dioxide (etCO2). Were recorded during startup and at 5, 10 and 15 minutes after the induction of anesthesia. Other measurements involved the volume of crystalloid infused in the first fifteen minutes and the requirement of vasoactive agents.

The analysis and validation of the data involved a univariate analysis of each variable for the qualitative variables in proportions and frequencies while for quantitative variables the analysis included measurements of central tendency and dispersion. In order to compare the characteristics of the two groups a bivariate analysis using the Fisher's exact test where all value of p less than 0.05 were considered significant..

RESULTS

Preoperative characteristics

All 60 patients could complete the study without complications. Group 1 were those who received propofol and ketamine, and group 2 those who received propofol and fentanyl.

The average age in the Group 1 was 38.6 +/- 12.8, with a minimum age of 18 and maximum of 61, while in Group 2, the average age was 37.23 +/- 13, with a minimum age of 18 years and a maximum of 58, the median age for Group 1 was 40 years and 38 years for Group 2.

The distribution of the gender in Group 1 was 63,2% women and 36,6% male, while the distribution by gender in Group 2 was 60% male and 40% female.

The average weight for Group 1 was 65.4 +/- 8.4 while for Group 2 was 68.7 +/- 11.0 for a minimum of 52 kg and maximum 82 for Group 1 and a minimum of 42 kg and maximum of 88 for Group 2.

In Group 1 which had more cases was general surgery with a 15% (n=9), the Group 2 general surgery with 10% group (n 6), followed by orthopedic services in the Group 1 were 13.3% (6) and in Group 2 were 8.3% (5).

No significant differences were found among the discriminated groups, by age, gender and weight; both populations were comparable in terms of all the variables.

In terms of diagnosis, the most common were cholelithiasis, 11.6% (n=7), uterine myomas 8.3% (n=5), ovary tumour, 5% (n=3), hemothorax, 3.3% (n=2), ganglion, 3.3% (n=2), distal radius fracture, 3.3% (n=2), and contraceptive methods 3.3% (n=2). Taking into account the procedures, the most common were cholecystectomy, 11.6% (n=7), followed by abdominal hysterectomy, 6.6% (n=4), ovary tumor resection, 5% (n=3), and radius osteosynthesis, 5% (n=3).

According to the ASA classification, 26.6% in Group 1 (n=16) were ASA I, and 36.6% in Group 2 (n=22); ASA II patients in Group 1 were 23.3% (n=14) and 13.3% in Group 2 (n=8).

Crystalloids were used in 100% of the cases in both groups, without significant differences. Vasoactive drugs were not used in any of the two groups.

For the maintenance of the airway the laryngeal mask was used in Group 1 in 20% (n=12) and orotracheal tube in 30% (n=18); in Group 2, 11.1% (n=4) used the laryngeal mask and 43.3% the orotracheal tube (n=26).

The most used muscle relaxant was vecuronium in both groups; for Group 1 were 26.6% and Group 2 were 38.3%, followed by non-use of muscle relaxation in Group 1 of 20% and 8.3% to Group 2. Sevoflourane dose for maintenance was comparable in both groups being 3% the dose most used 50% for Group 1 and 45% for Group 2.

The dose of remifentanyl for maintenance of 0.2 ups being 3% the dose most used 50% for Group 1 and 45% for Group 2.

The average dose of propofol for Group 1 was 158.6 +/- 19.7, with a minimum of 110 mg dose and a maximum of 190 mg, a mode of 150-160 mg, for Group 2 averaged 143.6 +/- 24.2, with minimum of 100 mg and 200 mg, a mode of 50 mg maximum dose.

The average use of ketamine in Group 1 was 57.13 +/- 11.14, minimum of 50 mg and maximum of 75 mg, the mode of 50 mg; In Group 2 of fentanyl, the average was 173.7 +/- 45 .2, with miniose 100 serage use of ketamine in Group 1 was 57.13 +

Midazolam was used in Group 1 in average dose of 2.75 +/- 0.44 with minimum dose of 2 mg and 3 mg maximum, being used higher doses in the group 2 with minimum of 2 mg and 4 mg maximum dose and on average 3.12 +/- 0.5 The mode for both was 3 mg.

Hemodynamic responses

The clinical and hemodynamic parameters were evaluated in both groups. To evaluate potential changes in heart rate (HR), arterial blood pressure (ABP), end-tidal carbon dioxide (etCO2) and oxygen saturation (SPO2).

The HR at time zero in Group 1 averaged 77, group 2 was 67 beats per minute, with a minimum of 45 in the Group 1 and 2 of 49. The maximum for Group 1 was 120 minute heart beats and for Group 2 was 88 beats per minute.

The patients in Group 1 experienced a greater difference in heart rate than those in group 2 in the minute 5 and 10. (Figure 1).

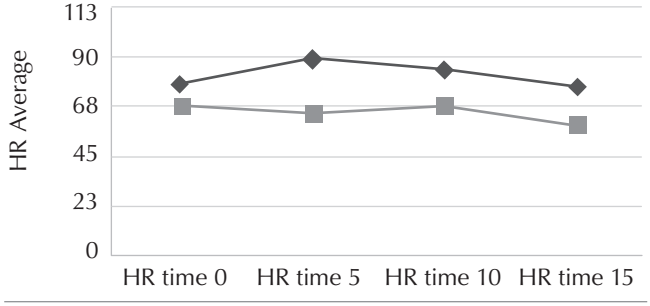

Figure 1. Variation in Heart Rate (HR)

The average blood pressure at the beginning was 124/77 mm Hg for Group 1 and Group 2 of 125/78 mm Hg, with a minimum 94/59 mmHg and maximum 157/96 mmHg in Group 1 and Group 2 minimum 96/44 mm Hg and maximum 148/99 mmHg. Arterial blood pressure increased in both groups, but for Group 1 to 5 min, at minute 10 and 15, with respect only to 10 min in Group 2. The mean arterial pressure (MAP) was in 89 mm Hg Group 1 and Group 2 to 90 mm Hg. Minimum and maximum blood pressure was 54-112 for Group 1 and group 2 was 60-114. In the 15 minute average in Group 1 was 70 to 66 in Group 2, with a minimum - maximum 55-118 mm Hg for a minimum - maximum of 50-90 in Group 2 and Group 1. (Figure 2)

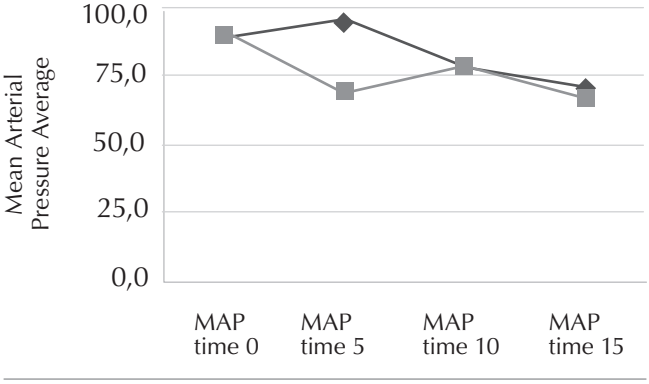

Figure 2. Variation in Mean Arterial Pressure (MAP)

Groups were comparable in terms of oxygen saturation (SPO2) there was no difference between in both groups. The average in the time zero in both groups was 95% and the minute 5, 10 and 15 to 98%.

The ETCO2 presents an average Group 1 in 5 min of 27 mm Hg and the Group of 24.13 Group 2 mm Hg, with a presentation of the minimum of 20 mmHg and maximum of 36 mmHg in Group 1 and group 2 minimum 12 mmHg and maximum 33 mmHg , which can be correlated with increased blood flow and episodes of tachycardia and hypertension associated with the use of ketamine in the 5 min in Group 1. In 10 min average for Group 1 is 29 and for Group 2 of 26.8, with a minimum of 23 and maximum of 36 for the 1 and the Group 2 for 22 minimum and maximum of 36 in 10 min. The trend is maintained in 15 min. (Figure 3)

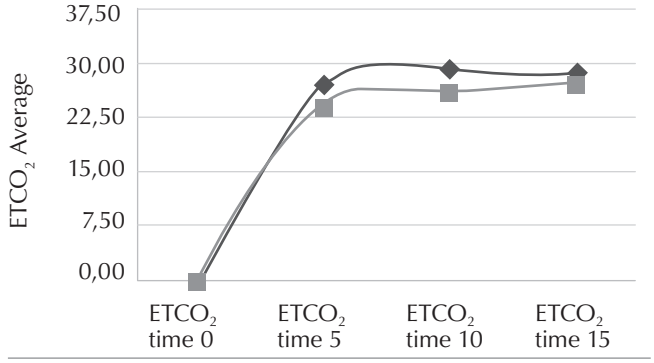

Figure 3. Variation in End-tidal Carbon Dioxide ($ETCO_2$)

The group that received propofol-fentanyl (Group 2) decreased significantly the heart rate during the procedure as compared to the propofol-ketamine group (Group 1) at the beginning, the minute 5, 10 and the 15 minutes during anesthetic induction. Both groups managed an average blood pressure similar at the Time 0 and minute 10, presenting a marked decrease in the minute 5 in the group that received propofol-fentanyl and a slight decline in 15 min. Both groups handled a value in pulse oximeter similar at the beginning and 5 min, showing a slight decrease in 10 min and 15 min in the group that received propofol-ketamine (Group 1). The End-tidal carbon dioxide (etCO2) during procedure in the Group that received propofol-fentanyl (Group 2) were apparently lower than those in the Group propofol-ketamine (Group 1) at the minute 5, 10 and 15 minutes.

BIVARIATE ANALYSIS

Bradycardia

The risk of bradycardia to the 5 min with propofol-fentanyl is seven times greater than with ketamine,

with statistically significant results (OR=7.2, 95% CI 1.81 - 64.4; p=0.05).

The risk of bradycardia to the 10 min with propofol-fentanyl is six times greater than with ketamine, with statistically significant results (OR=6.0, 95% CI 1.48 - 24.2; p=0.0007).

The risk of bradycardia to the 15 min with propofol-fentanyl is six times greater than with ketamine, with statistically significant results (OR=6.5, 95% CI 1.82 - 23.2; p=0,000).

Tachycardia

The risk of tachycardia at the 5 min with propofol-ketamine is 14 times greater than with propofol-fentanyl, with statistically significant results (OR=14.5; 95% CI 1.7 p=0,000)..ing p

The risk of tachycardia at the minute 10 with propofol-ketamine min is eight times greater than with propofol-fentanyl, with statistically significant results (OR=8.8, 95% CI 1.01 - 76.9; p= 0.02).

The association between tachycardia at the minute 15 with propofol-fentanyl is not statistically significant. There is one tendency with ketamine (OR 3.22 CI 95% 0.31-32.8 (p=0.30).

Hypotension

The risk of hypotension to the 5 min with Propofol - Fentanyl is 14 times greater than with ketamine, with statistically significant results (OR 14.5 CI 95% 1.7- 122 (p 0,000).

The association between hypotension with Propofol - Fentanyl 10 min is not statistically significant (OR 13.1 CI 95% 0.31-5.4 (p: 0.000).

The association between the 15 min hypotension with Propofol - Ketamina or Propofol - Fentanyl is not statistically significant. There is one tendency with ketamine (OR 1.15 CI 95% 0.40 - 3.34 (p: 0.50).

Hypertension

The risk of hypertension to the 5 min with Propofol-ketamine is eight times greater than with Propofol - Fentanyl, with statistically significant results (OR 8.82 CI 95% 1.01 - 76.9 (p: 0.02).

The association between hypertension to the min 10 with Propofol-ketamine or Propofol Fentanyl is not statistically significant.

There is one tendency with ketamine (OR 2.07 CI 95% 0.17- 24.1 (p:0.50).

The association between hypertension min 15 with Propofol-ketamine or Propofol-Fentanyl is the same and is not statistically significant (OR 1.0 CI 95% 0.05 - 16.7 (p: 0.75).

DISCUSSION

Anesthesia is born as a specialty by the need for control pain subsequently with their evolution we sought other perks as neurovegetative control, amnesia, hypnosis and the neuromuscular relaxation if necessary. Neurovegetative system is often associated with the hemodynamic control to maintain perfusion of different organs and their function (1,2,12). Hypotension is a common finding after induction of anesthesia, being the first 5 and 10 minute periods of greatest vulnerability. Reich and collaborators found some predictors of hypotension after induction of general anesthesia as most common finding during the first 10 minutes post-induction. Statistically significant multivariate predictors of hypotension during this time period were: 1. Patients ASA III-IV; 2. Baseline MAP < 70 mm Hg; 3. Older than 50 years; 4. Use of propofol during anesthetic induction; 5. Increase in the dose of fentanyl during induction. There is evidence that hypotension and hypertension during general anesthesia are independently associated with adverse outcomes in patients having both noncardiac and cardiac surgery (8).

The diagnosis of intraoperative hypotension is controversial approximately 140 definitions between different thresholds and time of presentation, definitions have been their applicability to different studies, no general consensus exists. Furthermore, studies published so far have used their own set of variables, since the findings influence the estimated associations of adverse events, varying data when applied to the data of the patients. In our study we consider low blood pressure greater than 30% in the blood pressure decrease average basis, with respect to the entrance to the operating room or the presence of TAM below 60 mmHg. Found statistically significant associations between post-induction hypotension and increased morbidity and mortality, resulted in increase of hospital stay (1, 2, 3, 4, 5, 6, 7, 8, 10, 12,13). Some studies have shown causation and hypotension, perioperative mortality to one year, for every minute of hypotension with less than 80 mm Hg tension figures, increases the risk of mortality by 3.6%, and increases the risk of stroke by 1.3%. The occurrence of intraoperative hypotension and development of ischemic stroke 10 days after surgery has been correlated.

Monk and colleagues note that mortality to one year increased by 3.6% per each minute systolic blood pressure was less than 80 mm Hg (10). Other studies have not found any causality, for short periods of time hypotension are tolerated in patients of advanced age (1,2,3,9). Bijker and collaborators found a relationship in the reduction of the mean arterial blood pressure greater than 30% of the initial value, statistically significant associated with the occurrence of postoperative stroke in patients undergoing non-cardiac, non-neurological surgery. It is a rare but serious complication reaching 0.1 - 3% accidents ischemic in general surgery and 10% in cardiac surgery, being responsible the hypoperfusion for 9% in cardiac surgery (9). For all these reasons the search for medicines that provide increased hemodynamic stability is a challenge for the anesthesiologist, as there is a medicine that meets all the conditions and/or benefits of general anesthesia.

The use of ketamine is not so common in operating rooms and leaves patients with certain characteristics because have sympathomimetic cardiovascular effects how elevations in heart rate and blood pressure.

In the present study, we found an association statistically significant in the development of bradycardia seven times higher in the Group of propofol-fentanyl in 5 min; at minute 10 and six times greater than with ketamine in the minute 15 (OR=7.2; 95% CI 1.81-64.4; p=0.05) (OR=6.01; 95% CI 1.48-24.2; p=0.0007) (OR=6.5; 95% CI 1.82-23.3; p=0.000). The risk of tachycardia was 14 times higher in the Group of propofol-ketamine per minute 5 that in the Group of propofol-fentanyl, being statistically significant (OR=14.5; 95% CI 1.7-122; p=0.002) in 10 min was 8 times higher in with ketamine than with fentanyl (OR=8.8; 95% CI 1.01-76.9; p=0.02). Perioperative hypotension during anaesthetic induction in minute 5 was 14 times higher in the Group of propofol-fentanyl than with ketamine and was statistically significant (OR=14.5; 95% CI 1.7-122; p=0,000). Perioperative hypotension in the minute 10 (OR 1.3 CI 95% 0.31-5.4 p:0.50) compared with the minute 15 (OR 1.15 CI 95% 0.40-3.34 p:0.50) this was not statically significant.

Hypertension with propofol-ketamine in the minute 5 was 8 times higher with respect to fentanyl being statistically significant (OR=8.82; 95% CI 1.01-76.9; p=0.02). In the minute 10 and minute 15 this was not statically significant (OR 2.07 CI 95% 0.17-24.1 p:0.50) (OR 1.0 CI 95% 0.05-16.7 p:0.75).

Sukhminder and collaborators reported that combination of propofol-fentanyl in total intravenous anesthesia (TIVA) had greater impact on older persons at the same doses than in young people, in our case the combination was used in patients 18 to 65 years and is not comparable to this study. Our findings are comparable and relevant with results of other studies, and are consistent with respect to the findings in the study of Mayer and colleagues were reported decrease in heart rate of the 9% with propofol-fentanyl in the study group compared with total intravenous anesthesia with propofol-ketamine; at the beginning of the surgery, they reported large hemodynamic changes in particular bradycardia up to 40 beats per minute (12.20). The opioids modulate the response to stress on a effect on the receptors in the hypothalamic-pituitary-adrenocortical axis, decreasing sympathetic tone and stimulating vagal activity.

Another finding of the study of Mayer is the elevation of heart rate in patients with propofol-ketamine, which may be given by the effect of ketamine sympathomimetic or response to stress during the manipulation of the airway. In our study of hypotension and bradycardia episodes were relevant in the Group of propofol-fentanyl in 5 min with statistically significant results and the discovery of hypertension and tachycardia in patients with propofol-ketamine in the minute 5 in hypertension and the minute 5, 10 and 15 in tachycardia. Smischney and collaborators as well as Hamzeh and collaborators reported in his study the use of propofol-ketamine mixture (ketofol) can allow better hemodynamic control (21, 22). It should be noted that the hypotension perioperative also depends on many other factors such as drug use and associated comorbidities. in this study as patients met inclusion criteria be ASA I- II, healthy patients or controlled systemic disease. Vasopressor were not used in any patient despite hypotension occurred in 5 minute and was fourteen times higher in Group 2. Another finding was declining and the difference in terms of the ETCO2 in patients managed with propofol-fentanyl with propofol-ketamine 5, 10 and 15 minutes, which may be due to the decrease in heart rate, preload and post-load.

The strengths of the study are framed in the statistically significant values, methodological rigor with which the data were taken, and that is the only study in this institution and in our midst with propofol-fentanyl vs propofol-ketamine. A greater number of studies to define which is the best anesthetic technique are required.

CONCLUSIONS

Anesthetic technique that generated more bradycardia The anesthetic technique that generated more bradycardia and hypotension was propofol-fentanyl, whereas the anaesthetic technique that generated more tachycardia and hypertension was propofol-ketamine.

The risk of bradycardia with propofol-fentanyl was higher than in the Group of propofol-ketamine (OR=7.2; 95% CI 1.81-64.4; p=0.05) being statistically significant.

The risk of tachycardia with propofol-ketamine was higher than in the Group of propofol-fentanyl (OR=14.5; 95% CI 1.7-122; p=0.002) being statistically significant.

The risk of hypotension with propofol-fentanyl was higher than in the Group of propofol-ketamine in the minute 5 after the induction (OR=14.5; 95% CI 1.7-122; p=0,000) was statistically significant.

The risk of hypertension with propofol-ketamine was higher than in the Group of propofol-fentanyl in the minute 5 after the induction (OR=8.82; 95% CI 1.01 - 76.9; p=0.02) was statistically significant.

A higher value of carbon dioxide found in exhalation in the Group of propofol-ketamine than in the Group of propofol-fentanyl, relationship that was maintained at 5, 10 and 15 minutes.

RECOMMENDATIONS

Taking into account the results of the present study is recommended to take into consideration and caution the use the propofol-fentanyl in patients with low tolerance decreased mean arterial pressure, heart rate during the period of anesthesia induction. Likewise, it is recommended that patients receiving propofol-ketamine can tolerate increases in their average blood pressure and heart rate.

You must be very cautious in the choosing induction drugs in patients with significant co-morbidities which do not tolerate marked changes in their haemodynamic variables such as hypertensive patients with a history of coronary artery disease, kidney disease, or cerebrovascular disease.

Proposals for the service of Anesthesiology of the institution generate rcommendations for the induction of general anesthesia, with the aim of decreasing the incidence of long periods of significant hemodynamic alterations in patients.

We suggest to carry out new studies to measure the medium-term effect of hemodynamic changes intraoperative variables of morbidity and mortality in patients who are undergoing surgery in Hospital Simon Bolivar, including patients ASA III-IV who are prone to hemodynamic disturbances during general anesthesia.

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